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(19) **United States**(12) **Patent Application Publication****Daya et al.**(10) **Pub. No.: US 2021/0348131 A1**(43) **Pub. Date: Nov. 11, 2021**(54) **VIRAL CLEARANCE BY LOW PH HOLD****Publication Classification**(71) Applicant: **Regeneron Pharmaceuticals, Inc.**,
Tarrytown, NY (US)(72) Inventors: **Jena Daya**, Brandon, VT (US); **Valerie Ann Cusick**, Whitehouse Station, NJ (US); **John Mattila**, Nyack, NY (US)(51) **Int. Cl.****C12N 7/00** (2006.01)**C07K 1/14** (2006.01)**C07K 16/10** (2006.01)(52) **U.S. Cl.**CPC **C12N 7/00** (2013.01); **C12N 2740/13063** (2013.01); **C07K 16/1036** (2013.01); **C07K 1/14** (2013.01)(21) Appl. No.: **17/317,602**(22) Filed: **May 11, 2021****Related U.S. Application Data**

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(57)

ABSTRACT

Methods for viral clearance using low pH hold based on a statistical design of experiment are provided. Several factors are evaluated to characterize the impacts of a low pH hold step for virus inactivation, including the factors of pH conditions, conductivity conditions, protein type, temperature, acid titrant, spike timing, and post-spike filtration. In addition to the effect of pH on virus inactivation, an increase in ionic strength through manipulating the conductivity can be a key component that influences virus inactivation kinetics.

